PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application of: Stephen A. Johnston et al Serial No. 10/023,437 Filing Date: December 17, 2001 Art Unit: 1645 Examiner: Vanessa L. Ford Methods and Compositions for Vaccination Comprising Nucleic Acid and/or Polypeptide Sequences of Chlamydia	CERTIFICATE OF EFS WEB FILING I hereby certify that this correspondence is being electronically filed via the USPTO Electronic Filing System (EFS Web) on this 27th day of June, 2008. /Marlene Kubiak/ 06/27/08 Marlene Kubiak Date

APPELLANTS' BRIEF ON APPEAL

Board of Patent Appeals and Interferences
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Brief is submitted in accordance with 37 C.F.R. § 41.37 and is submitted with the required fee under 37 C.F.R. § 41.20 of $255.00.

REAL PARTY IN INTEREST

In accordance with 37 C.F.R. §41.37(c)(1)(i), the real parties in interest are (1) Auburn University, by assignment from the inventors dated February 15, 2002, recorded in the U.S. Patent and Trademark Office on April 1, 2002 at Reel 012772, Frame 0866; and (2) Board of Regents, The University of Texas System, by assignment from the inventors dated February 8 and 19, 2002, recorded at the U.S. Patent and Trademark Office on March 29, 2002 at Reel 012765, Frame 0225.

RELATED APPEALS AND INTERFERENCES

In accordance with 37 C.F.R. §41.37(c)(1)(ii), it is hereby stated that there are no other prior or pending appeals, interferences or judicial proceedings known to Appellant,

Appellant's legal representative, or assignee, which may be related to, directly affect, or be directly affected by or have a bearing on the Board's decision in the present pending Appeal.

STATUS OF CLAIMS

In accordance with 37 C.F.R. §41.37(c)(1)(iii), the following is a statement of the status of the claims.

Claims 1-91, 93 and 96-103 stand canceled.

No claims stand allowed.

Claims 92, 94, 95 and 104-121 stand rejected.

Claims 92, 94, 95 and 104-121 are appealed.

Claims 92, 94, 95 and 104-121 have been rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter or, in the alternative, under 35 U.S.C. § 112, ¶1, for lack of enablement. Claims 104-106 have been rejected under 35 U.S.C. § 112, ¶2, for failing to particularly point out and distinctly claim the subject matter which applicants regard as their invention.

STATUS OF AMENDMENTS

Prior to this Appeal Brief, applicants have not submitted an Amendment in response to the Office Action mailed January 28, 2008. Applicants are willing to make the suggested corrections to obviate the rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, ¶2, once the issues involving enablement under 35 U.S.C. § 112, ¶1, are resolved through the present appeal.

SUMMARY OF CLAIMED SUBJECT MATTER

In accordance with 37 C.F.R. §41.37(c)(1)(v), the following is a summary of the claimed subject matter.

The claimed subject matter relates to a method of immunizing an animal through administering a *Chlamydia psittaci* antigen to an animal in an amount effective to induce an immune response. The claimed subject matter is more particularly directed to specific sequence listings. Sequence listings 7, 9, 13, 23 and 27 are particularly claimed. Specific immunogenic sequences are important because of widespread human and animal infections by the genus *Chlamydia*. For example, *Chlamydia psittaci* infections in cattle cause mastitis, infertility and

undesired abortion. A primary economic impact of *Chlamydia* in dairy cattle is the loss of milk production and quality. Thus, an effective treatment for *Chlamydia* bacterial infections in human and other vertebrate animals would be of clinical and economic importance. The present invention provides compositions and methods for the immunization of vertebrate animals, including humans, against infections using nucleic acid sequence and polypeptides elucidated by screening *Chlamydia psittaci*. This distinctly claimed method is useful for immunization against *Chlamydia psittaci* bacterial infections.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

In accordance with 37 C.F.R. §41.37(c)(1)(vi), the following is a concise statement of each ground of rejection presented for review.

Appellants respectfully request review of the rejection of claims 92, 94, 95 and 104-121 under 35 U.S.C. §112, ¶1, for lack of enablement.

ARGUMENT

In accordance with 37 C.F.R. §41.37(c)(1)(vii), Appellants now set forth their contentions with respect to each ground of rejection presented for review pursuant to 37 C.F.R. §41.37(c)(1)(vi), and the basis therefor.

In accordance with 37 C.F.R. §41.37(c)(1)(vii), the claims involved in the Appeal are set forth in the attached claims appendix. In accordance with 37 C.F.R. § 41.37(c)(1)(ix), an appendix containing copies of evidence submitted pursuant to 37 C.F.R. § 1.132 is attached hereto.

The present application has endured a long and tortuous path during initial prosecution. After many fruitless amendments suggested by the Examiners,[1] and later rejected; and in light of stark contradictions by the Examiners in substantive positions, appellants now are compelled to turn to the Board for review and consideration.

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[1] Appellants have prosecuted the present application before several Examiners, particularly Biotechnology Patent Examiner Vanessa L. Ford, Primary Examiner Mark Navarro, Primary Examiner Nita Minnifield, Supervisory Examiner Lynette R.F. Smith, Supervisory Examiner Jeffrey Siew, and Supervisory Examiner Shannon Foley. Accordingly, appellants will refer to decisions, remarks and Office Actions issued by "the Examiners."

A. The Outstanding Rejection Under 35 U.S.C. § 101

Appellants acknowledge that there is an outstanding rejection under 35 U.S.C. § 101 regarding whether the claims are directed to non-statutory subject matter. The Office Action dated January 28, 2008 indicates that "This rejection may be obviated, if the claims are amended to an 'isolated or purified' *Chlamydia psittaci* antigen." Appellants intend to make the proposed amendment when the enablement issues are resolved through this appeal.

B. Claims 92, 94-95, 102-121 Are Enabled Under 35 U.S.C. § 112, ¶1

Appellants frame the enablement issue on appeal as follows: *Does the specification provide enablement for a method of immunizing an animal in an amount effective to induce an immune response against Chlamydia psittaci; wherein the Chlamydia psittaci and the antigen comprise the amino acid or polypeptide sequences as set forth as Sequence ID Nos. 7, 9, 11 or 13?*

The purpose of the requirement that a specification describe the invention in such terms that one skilled in the art can make and use the claimed invention is to ensure that the invention is communicated to the interested public in a meaningful way, MPEP § 2164. The information contained in the disclosure of an application must be sufficient to inform those skilled in the relevant art how to make and use the claimed invention, Id. To comply with 35 U.S.C. § 112, first paragraph, it is not necessary to "enable one of ordinary skill in the art to make and use a perfected commercially viable embodiment absent a claim limitation to that effect." CFNT, Inc. v. Yieldup International Corp., 349 F.3d 1333, 1338, 68 USPQ 2D 1940, 1944 (Fed. Cir. 2003). Detailed procedures for making and using the invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention, MPEP § 2164.

Any analysis of whether a particular claim is enabled by the disclosure in an application requires the determination of whether that disclosure, when filed, contains sufficient information regarding the subject matter of the claims as to allow one skilled in the pertinent art to make and use the claimed invention, MPEP § 2164.01. This requirement has been interpreted to require that the claimed invention be enabled that any person skilled in the art can make and use the invention without undue experimentation, In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). It is well settled that a patent need not teach, and preferably omits, that which is well known in the art, In re Buchner, 929 F.2d 660, 661, 18 USPQ 1331, 1332

(Fed. Cir. 1991). Determining enablement is a question of law based on underlying factual findings, In re Vaeck, 947 F.2d 1488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991).

In re Wands sets out the factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill in the art; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure, In re Wands, 858 F.2d at 737. Moreover, compliance with the enablement requirement of 35 U.S.C. § 112, ¶1, does not turn on whether an example was disclosed, MPEP § 2164.02. In other words, lack of working examples or lack of evidence that the claimed invention works as described should never be the sole reason for rejecting the claimed invention on grounds of lack of enablement, Id.

In accordance with the principles of compact prosecution, if an enablement rejection is appropriate, the first Office Action on the merits should present the best case with all the relevant reasons, issues and evidence so that all rejections can be withdrawn if applicant provides appropriate convincing arguments and/or evidence in rebuttal, MPEP § 2164.01. In other words, the Examiner should always look for enabled, allowable subject matter and communicate to applicant what that subject matter is at the earliest point possible in the prosecution of the application, Id. (emphasis in original).

> Here, the Examiners asserted early and often that:
>
> "... The claims while being enabling for a method of immunizing an animal comprising providing to the animal; at least one Chlamydia antigen corresponding to Sequence ID No. 9 or No. 7 and further comprising a second Chlamydia antigen corresponding to Sequence ID No. 11 or No. 13 ..." (*see*, e.g., Office Action mailed 05/31/05 at p. 3).

This statement led the appellants to believe that a method of immunizing an animal in an amount effective to induce an immune response against *Chlamydia psittaci*; wherein the *Chlamydia psittaci* antigen comprises the amino acid or polypeptide sequence as set forth in Sequence ID Nos. 7, 9, 11 and 13 was clearly enabled. It was not until seven years into the prosecution that the issue involving whether or not a single sequence was enabled was first identified by the

Examiner. This convoluted and extrapolated prosecution of the present application is exactly the opposite of a "compact prosecution" discussed in MPEP § 2164.04. Moreover, even though this enablement issue was identified extremely late in the prosecution, overwhelming evidence demonstrates that immunization with a single amino acid polypeptide sequence is enabled.

C. History of Prosecution

Appellants filed an application for patent on December 17, 2001, claiming priority to provisional application No. 60/255,839. An initial Election/Restriction was issued on October 2, 2003, but was later withdrawn. A second Election/Restriction was issued on February 12, 2004 after an interview with the Examiners. The claims were restricted into eight groups, and on April 14, 2004, appellants elected claims directed to methods of immunizing an animal involving Sequence ID No. 9 as the species. Sequence ID Nos. 6-8 were also incorporated into the species selection because Sequence ID No. 8 is a full length polynucleotide sequence encoding the polypeptide sequence of primary elected Sequence No. 9. Sequence ID No. 6 disclosed an antigenic polynucleotide fragment of Sequence ID No. 8, and Sequence ID No. 7 is a polypeptide transition of the polynucleotide sequence of Sequence No. 6. Applicants specifically noted the interrelationship between the various Sequence ID Nos. early on in this prosecution:

> "Applicants would point out that Sequence ID No. 9 comprises, as amino acids 258-406, the 149 amino acid Sequence ID No. 7. Further, Sequence ID No. 8 (which encodes Sequence ID No. 9), comprises, as nucleic acid 717-1220, the 449 nucleic acids of Sequence ID No. 6 (which encodes Sequence ID No. 7). Therefore, in view of the election of species of antigens or antigenic fragments having a sequence of Sequence ID No. 9, claims directed to antigens of Sequence ID No. 7 and antigenic fragments thereof, polypeptides of Sequence ID No. 8 and fragments thereof, and polypeptides of Sequence ID No. 6 and fragrance thereof are sub-specific claims within the specific claims directed to antigens of Sequence ID No. 9 or antigenic fragments thereof. No additional search is required to search Sequence ID No. 7 if Sequence No. 9 is searched and no additional search is required to search Sequence ID No. 6 if Sequence ID No. 8 is searched." (*see*, Amendment and Response to Restriction Requirement of 04/14/04 at pp. 10-11).

On July 9, 2004, the Examiners issued another Election/Restriction restricting the claims into three classes and requiring election of a single species of bacteria. Appellants responded on August 9, 2004 by filing an election with traverse and elected to prosecute the *Chlamydia psittaci* bacteria and also electing to prosecute Sequence ID No. 13 as the claimed

"second *Chlamydia* antigen." Again, appellants specifically noted the interrelationships in the grouping of the sequence ID numbers:

> "Applicants would point out that Sequence ID No. 13 comprises the amino acid sequence of Sequence ID No. 11. Therefore, in view of the election of the species of antigens or antigenic fragments having a sequence of Sequence ID No. 13, claims directed to antigens of Sequence ID No. 11 and antigenic fragments thereof, are sub-specific claims within the specific claims directed to antigens of Sequence ID No. 13 or antigenic fragments thereof. No additional search is required to search Sequence ID No. 11 if Sequence ID No. 13 is searched." (*see*, Amendment and Response to Restriction Requirement of 08/09/04 at pp. 10-11).

On November 10, 2004, the Examiners issued a first substantive Office Action rejecting the pending claims for lack of enablement under 35 U.S.C. § 112, ¶1, because of the claim language "or an antigenic fragment thereof." The Examiner asserted that there is insufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention because claims with the language recited above broadly include any number of deletions or substations and fragments of any size. The Examiners also issued a rejection under 35 U.S.C. § 102 over the Graffais reference. Appellants responded to the non-final Office Action on March 10, 2005 traversing the rejection under § 102 and also traversing the enablement rejection. With respect to the enablement rejection, applicants noted that the specification specifically defines an "antigenic fragment" as eliciting an immune response. Moreover, the specification provides specific sequences of exemplary antigenic fragments (e.g., Sequence ID Nos. 6 and 7) and teaches that conservative substitutions may be made. Appellants also submitted a Declaration under 37 CFR § 1.132 from Akira Takashima, a person of ordinary skill in the art, which is attached hereto as Exhibit A in the evidence appendix. Briefly, the Declaration indicates that a person having ordinary skill in the art would recognize that the specification demonstrates both a full length sequence (e.g., Sequence ID No. 9) and an antigenic fragment of that sequence (e.g., Sequence ID No. 7) that can immunize an animal. The Declaration concluded that based on the reported results in the specification, there would be likely other antigenic fragments that could readily be identified through routine experiments by a person having ordinary skill in the art.

The Examiners issued a final Office Action on May 31, 2005 maintaining all rejections. The Examiners specifically stated:

> "The rejection was on grounds that the claims **while being enabling for a method of immunizing an animal comprising providing to the animal; at least one Chlamydia antigen corresponding to SEQ ID No. 9 or No. 7** and further comprising a second Chlamydia antigen corresponding to SEQ ID No. 11 or No. 13 does not reasonably provide enablement for all antigenic fragments of SEQ ID Nos. 7, 9, 11 or 13." (*see*, Office Action mailed 05/31/05 at p. 3) (underline in original; bold added).

It must be specifically noted that the Examiners admitted that the claimed method was enabling for immunizing an animal with full length Sequence ID Nos. 9 or 7 further with a second antigen comprising Sequence ID Nos. 11 or 13. On August 31, 2005, appellants submitted amended claims to recite: "A *Chlamydia psittaci* antigen having a Sequence ID No. (e.g., 7, 9, 11 or 13)." This amendment was made specifically to the admission in the 05/31/05 Final Office Action that "the specification was enabling for *C. psittaci* antigens having sequences corresponding to Sequence ID Nos. 7, 9, 11 and 13. The limitation was also asserted by applicants to overcome the Graffais 35 U.S.C. § 102 rejection. However, in an Advisory Action dated September 29, 2005, the Examiners refused to enter the amendments because "The claims as amended would require further consideration and would require new searches," even though the Examiners subsequently point out that the claims were narrowed to "having the sequence of Sequence ID No. 9" from "have the sequence of Sequence ID No. 9 or antigenic fragment thereof comprising at least 25 contiguous residues of Sequence ID No. 9." (*see*, Advisory Action attachment mailed 09/29/05 at p.2). In response, appellants filed a Request for Continued Examination on October 28, 2005, re-submitting the amendments made in the August 31st Response.

On January 25, 2006, the Examiners issued an Office Action entering appellants' submission of October 31, 2005 amending claims 25, 39, 41-42 and 83; adding claims 92-107; canceling claims 1-24, 28, 40, 46-49, 63-73, 75, 82, 84-91; and noting withdrawal of claims 26-38, 50-61 and 76-81. The Office Action specifically identifies that claims 92, 104, 107, 110 and 113 are allowed both in the Summary of the Office Action and on p. 13 of the Office Action (p. 13 also noted allowance of claim 93). The Examiners issued an enablement rejection for newly submitted claims 96-103, again on the grounds that fragments and variants of the claimed sequences are not enabled, and maintained the same rejection for claims 25, 39, 41-45, 74 and 83. In making this enablement rejection (in 2006 for an application filing date of 2001), the

Examiners relied on references from 1984 and 1991 to support their rejection. Significantly, the Examiners again state:

> "The rejection was on the grounds that the claims **while being enabling for a method of immunizing an animal comprising providing to the animal: at least one Chlamydia antigen corresponding to SEQ ID No. 9 or SEQ ID No. 7** and further comprising a second Chlamydia antigen corresponding to SEQ ID No. 11 or SEQ ID No. 13 does not reasonably provide enablement for all antigenic fragments of SEQ ID. 7, 9, 11 or 13 encompassed by the claims that can be used in the claimed method." (*see*, Office Action mailed 01/25/06 at pp. 2-3) (bold added; underline in original).

The January 25, 2006 Office Action also maintained the 35 U.S.C. 102 rejection over Graffais for claims 25, 39, 41-45, 74, 83 and newly submitted claims 100 and 103.

In response, appellants requested a personal interview and submitted a proposed Amendment and Remarks on April 7, 2006. The interview was conducted on April 11, 2006. A final Amendment was submitted on May 16, 2006. The May 16, 2006 Amendment supplemented the April 7, 2006 response, and amended claims 25, 41, 42 and 96-103. Subsequent to suggestions made during the interview, the claims were amended to include the limitation "... wherein an amount effective is at least a nine amino acid fragment of Sequence ID No. (7, 9, 11, 13)." Appellants also argued each factor under In re Wands, 8 USPQ2d 1400, and indicated the existence of working examples present in the specification. Appellants specifically stated:

> "Working examples are found in the instant specification. **The present specification demonstrates that the 443 amino acid polypeptide of Sequence ID No. 9 and the 100 amino acid polypeptide of Sequence ID No. 13 can be used to immunize an animal. The specification also demonstrates that the 149 amino acid fragment (Sequence ID No. 7) with Sequence ID No. 9 and a 41 amino acid fragment (Sequence ID No. 11) and Sequence ID No. 13 can be used to immunize an animal.** Identification of the protective genes is described on pp. 64-80 in Examples 1-6 and illustrated in Figs. 1-6. The claims for fragments and full length DNA polypeptide sequences of the protective genes are based on the identification of protective DNA fragments of the Chlamydia psittaci genes in the approach outlined in the above examples. Specific evidence for the mouse protective effect is presented in Figs. 5 and 6 of Sequence ID No. 6 (Sequence ID No. 6 is CP4 No. 1), which is the DNA fragment corresponding to claimed polypeptide Sequence

> ID No. 7." (*see*, Supplemental Response and Amendment of 05/16/06 at p. 20) (emphasis added).

Appellants also traversed the 35 U.S.C. § 102 rejection by arguing that the Graffais contribution is merely the sequence of the entire *Chlamydia pneumonia* genome, and does not provide any vaccines or useful teachings on how to obtain vaccines. Moreover, the Graffais reference shows no protective capacity of the identified homologs.

On July 28, 2006, the Examiners issued yet another Office Action. The Examiners withdrew allowance of claims 92, 104, 107, 110 and 113 and rejected all pending claims. The Examiner stated for the third time:

> "The rejection under 35 U.S.C. § 112, first paragraph is maintained for [claims] 92 and 96-99 for the reasons set forth on pages 2-7, ¶4 of the Final Office Action. The rejection was on the grounds that the claims **while being enabling for a method of immunizing an animal comprising providing to the animal; at least one Chlamydia antigen corresponding to Sequence ID No. 9 or Sequence ID No. 7 and further comprising a second Chlamydia antigen corresponding to Sequence ID No. 11 or Sequence ID No. 13** does not reasonably provide enablement for variants of the Sequence ID No. 7, 9, 11 or 13 encompassed by the claims that can be used in the claimed method." (*see*, Office Action mailed 07/28/06 at p. 2) (bold added, underline in original).

On page 9 of the Office Action, the Examiners take issue with the word "comprising" as being open ended and takes the position that all claims including the word "comprising" read on sequences less than the full length sequence. The Examiners then offered a new grounds for rejection under 35 U.S.C. § 112, ¶¶1 and 2, regarding the amended claims, and made at least three 35 U.S.C. § 112, ¶2, rejections on unamended, but previously allowed, claim 92. The Examiners also rejected all the previously allowed claims under 35 U.S.C. § 112, ¶2, stating:

> "The preamble of claim 92 recites a 'method of immunizing ...'. Claim 92 also recites '... preparing a Chlamydia antigen ...". It is unclear what applicant intends by the step of preparing an antigen and a method of immunizing. Clarification and/or correction is required."

Finally, the Examiners issued a new rejection under 35 U.S.C. § 102 regarding an abstract from the named inventors, Dr. Bernhard Kaltenboeck. Nowhere did the Examiners address

appellants' careful analyses under In re Wands, thus implicitly acknowledging the presence of the specific working examples.

On October 17, 2006, appellants conducted a telephonic interview with the Examiners. During the interview, claims 96-103 were discussed relative to the rejection under 35 U.S.C. § 112, ¶1, for enablement. The Examiners confirmed that claims 92-95 and claims 104-115 were not rejected under 35 U.S.C. § 112 for enablement. Instead, the enablement rejection applied specifically to claims 96-103 which described either variants or fragments of a particular sequence ID number. Appellants and the Examiners also discussed how to obviate the other 112, ¶¶1 and 2 rejections from the July 28, 2006 Office Action.

On October 27, 2006, appellants submitted an Amendment canceling claims 35, 39, 41-45, 83 and 96-103. Claims 92, 94 and 95 were amended and new claims 116-121 were added. Appellants responded to all rejections raised by the Examiners in the previous Office Action, including the § 102 rejection based on the Kaltenboeck disclosure. It was appellants' position that the cancellation of the claims and the amendments to obviate the 35 U.S.C. § 112 rejections, along with the arguments traversing the § 102 rejection, placed the application in allowance, particularly in light of the previous identification of allowable subject matter in claims 92, 104, 107, 110 and 113.

However, on February 8, 2007, the Examiners issued another non-final Office Action. In this Office Action, the rejections under 35 U.S.C. § 112, ¶2, and under 35 U.S.C. § 102 were withdrawn. The Examiners now issued another new grounds for rejection under 35 U.S.C. § 112, ¶1, for failure to comply with the enablement requirement. The Examiners asserted:

> "The instant specification discloses in Examples 5-12 experimental examples using *Chlamydia* nucleic acid molecules and polypeptides used to immunize animals. The specification refers to Figs. 4-8 which disclose the data from the various experimental examples. Regarding Fig. 5, which are the results of protection assays of testing individual gene fragments in found [sic] 4 (page 15), the specification teaches that protection was scored as lung weight relative to the average of the vaccinate, maximum protection, positive control (vaccinated = 1) and the non-vaccinated, challenged, maximum disease, negative control (challenged = 0). It is unclear as to what applicant intends by the data presented in Fig. 5. The instant specification provides data in terms of maximum protection. Applicant does not present an unvaccinated control. Thus, one of skill in the art cannot interpret applicant's data as set forth regarding protection assays with data from an unvaccinated control. It is

> unclear as to what the data present in Fig. 5 actually discloses. The skilled artisan cannot drawn in [sic] conclusive evidence from the data presented in the instant specification." (*see*, Office Action mailed 02/08/07 at pp. 4-5) (emphasis added).

The Examiners also indicated that the specification fails to teach how the data in Fig. 5 correlates to protection assays and would require undue experimentation for a person having ordinary skill in the art. This position is contradictory to the Examiners' numerous previous assertions that a method for immunizing an animal is enabled.

Appellants responded on April 18, 2007 and submitted a Declaration of one of the named inventors, Dr. Bernhard Kaltenboeck, under 37 C.F.R. § 1.132, ¶2. That Declaration is included in the evidence appendix as Exhibit B. Dr. Kaltenboeck declared that Fig. 5 was clear and that an unvaccinated control was presented. The "challenged" group was a non-vaccinated, negative control as it provides a relative protection score which is completely unexposed to *Chlamydia psittaci*. Appellants stated in their Remarks:

> "[The 'challenged' group] is a control that is not vaccinated and that is not subject to the claimed genetic fragrance and, therefore, provides a base line for protection when exposed to *Chlamydia*."

On June 29, 2007, the Examiners issued a Final Office Action. The Examiners indicated that applicants provided a "great description" as to how the experimental assays were performed in the form of Dr. Kaltenboeck's Declaration to arrive at the data presented in Fig. 5. Presumably, the Remarks and Declaration of Dr. Kaltenboeck obviated the Examiners' previous concerns about unprovided unvaccinated controls. However, the Examiners felt that the data in Fig. 5 and the Declaration presented by Dr. Kaltenboeck somehow failed to provide a correlation between data presented in the specification and the claimed sequence ID numbers. Apparently, the Examiners felt that it is unclear as to which gene fragments (designated with CP4#1-14, i.e., *Chlamydia psittaci* Round 4 experiments Nos. 1 through 14) on Fig. 5 correspond to which sequence ID numbers recited in the claims and how to correlate the sequence ID numbers recited on page 75 of the specification with the "CP4#" numbers. Thus, the Examiners maintained rejection under 35 U.S.C. § 112, first paragraph, for enablement, although now different reasoning was given:

> "Taken together, it is unclear as to which antigens (SEQ ID Nos.) were used to generate the data presented in Figure 5 of the instant specification. Therefore, it is unclear as if the antigens used in the experimental examples actually correlate to the data presented in Fig.

> 5 or more importantly it is unclear as to whether the antigens recited in the claimed method were used in the experimental examples." (*see*, Final Office Action mailed 06/29/07 at p. 8).

Appellants submitted a Response after Final Rejection on August 8, 2007 submitting a second Declaration of Dr. Bernhard Kaltenboeck which is annexed hereto as Exhibit C to the evidence appendix. This Declaration clarified Fig. 5 and correlated the CP4# with the SEQ ID numbers. Moreover, the Declaration and Response make it clear as to which SEQ ID numbers are used to generate the data presented in Fig. 5.

However, on September 19, 2007, an Advisory Action was issued maintaining the rejection under 35 U.S.C. § 112, ¶2, for enablement. The Examiners specifically stated:

> "On the outset, it appears that applicant is enabled for some embodiments of the claimed method of immunizing an animal comprising administering a Chlamydia antigen. Unfortunately, the second Declaration submitted by Dr. Bernhard Kaltenboeck filed August 8, 2007 is insufficient to overcome the rejection. This Declaration does not clarify or correlate the data in Fig. 5 to the specification in the manner that the Office can appreciate the correlation. ... It cannot be ascertained from what is presented in the instant specification in the two Declarations submitted by Dr. Bernhard Kaltenboeck as to what antigens were administered to the animals and [what] protection was provided." (Advisory Action mailed 09/19/07 at p. 6-7) (emphasis added).

The Examiners requested that applicant contact the Examiner to schedule an in-person or telephonic interview to explain the invention further. Accordingly, on October 23, 2007, applicant's attorney and the named inventor, Dr. Bernhard Kaltenboeck, conducted an interview with the Examiners. During the interview, Dr. Kaltenboeck and applicant's attorney answered clarifying questions from the Examiners as to how the sequence ID numbers relate to the findings demonstrated in the figures, tables and examples of the original application. As an aid, a chart was provided (Exhibit D in evidence appendix) to demonstrate, with complete specificity, how particular protective *Chlamydia psittaci* fragment numbers in Fig. 5 of the specification correlate to the CP4# designations in Fig. 6 in Table 2 of the specification (*see*, Exhibit D to the evidence appendix). The chart also demonstrates how one CP# correlates to separate SEQ ID numbers. Dr. Kaltenboeck also explained the experimental strategy that led to the identification of plasmids containing the protective *Chlamydia psittaci* genes and detailed the experimental procedure to the Examiners. Applicants respectfully emphasized to the Examiners that a person having ordinary skill in the art understands that DNA vaccination with a nucleotide

sequence will also mediate protection conferred by vaccination with the corresponding protein sequence, since the nucleotide sequence is translated intracellularly into the protein sequence before providing a protective response. On October 26, 2007, applicants filed an Amendment providing a summary of the interview and attempted to clarify any confusion by submitting the table used in the interview (i.e., Ex. D). The Amendment also contained a Request for Continued Examination.

On January 28, 2008, another Office Action was issued by the Examiners. This Office Action included a new ground of rejection under 35 U.S.C. § 101 and also maintained the enablement rejection for claims 92, 94-95 and 104-121. However, again, the enablement rejection contained a new twist. With respect to enablement, the Examiners specifically stated:

> "The specification has shown enablement for immunizing cattle with a pool of 14 DNA genes. See Example 8 in Table 4 of the instant specification. The specification has also shown enablement for a genetic vaccine comprising a pool of 5 protected full length genes and/or gene fragments isolated in the gene screening process. **The instant specification has further shown enablement for a protein vaccine which comprises full length *Chlamydia psittaci* proteins and/or protein fragments**. See Example 9 of the specification. It should be noted that it is unclear as to whether the genetic vaccine disclosed in Example 9 comprises a pool of full length genes or gene fragments or a combination thereof. ... It is unclear as to which specific genes and which specific proteins are present in the vaccine compositions of Examples 8 and 9 of the instant specification. ... Thus, the specification discloses a method of immunizing animals comprising a pooled DNA vaccine and *not a method of immunizing an animal comprising administering a Chlamydia psittaci protein vaccine comprising administering **one single** Chlamydia psittaci* antigen as recited in the instant claims." (*see*, Office Action mailed 01/28/08 at pp. 3-4) (bold added, italics and underlining in original).

Thus, it appears that the Examiners' rejections now turn on whether a working example was disclosed, contrary to MPEP § 2164.02. Subsequently, the Examiners, Supervisory Examiner, appellants' attorney and named inventor, Bernhard Kaltenboeck, conducted an in person interview regarding the enablement on the record. Agreement was not reached and appellants subsequently filed a Notice of Appeal regarding rejected claims 92, 94-95 and 104-121.

D. The *Wands* Factors Demonstrate Enablement Under 35 U.S.C. § 112, ¶1

The appealed claims are narrowly directed to a method of immunizing an animal comprising the step of: administering a *Chlamydia psittaci* antigen to an animal in the amount effective to induce an immune response against *Chlamydia psittaci*; wherein the *Chlamydia psittaci* antigen comprises the amino acid sequence as set forth as SEQ ID No. 7. The dependent claims are more narrow claiming a method that further comprises administering a second *Chlamydia psittaci* antigen to an animal in an amount effective to induce an immune response against *Chlamydia psittaci*; wherein the second *Chlamydia psittaci* antigen comprises the amino acid sequence set forth as (Sequence ID Nos. 9, 11, 13, 17, 23 or 27), *see*, claims 94-95. As noted, SEQ ID No. 7 is a positively identified antigenic fragment of SEQ ID No. 9.

The appellants are at a complete loss as to why claims 94 and 95 are not enabled since those claims are directed to administering at least two separate antigens, and are not directed to administering a single antigen as the Examiners assert in the most recent Office Action of January 28, 2008. The non-allowance of claims 94-95 for non-enablement are made even more vexing in light of the Examiners' continued recitation that:

> "... The claims while being enabling for a method of immunizing an animal comprising providing to the animal; at least one Chlamydia antigen corresponding to Sequence ID No. 9 or No. 7 and further comprising a second Chlamydia antigen corresponding to Sequence ID No. 11 or No. 13 ..."

See, e.g., Office Actions of 05/31/05, 01/25/06 and 07/28/06 cited above.

In the instant case, the nature of the invention is a method of immunizing an animal comprising administering to the animal a *Chlamydia psittaci* antigen having a specific SEQ ID number in an amount effective to induce a protective immune response against *Chlamydia psittaci*. Prior art antibiotic treatment for *Chlamydia* infection is not practical and conventional vaccines are inconsistent. Therefore, a vaccine for the prevention of the disease in animals is desirable.

The application also includes working and prophetic examples. The inventors used expression library immunization (ELI) for identified vaccine candidates in the present application. The goal was to identify, among all *Chlamydia psittaci* proteins, the polynucleotide and polypeptide fragments that elicited protective immunity. In order to identify the particular sequences or fragments that were advantageous, the inventors conducted a series of experiments

with mice as detailed in Fig. 5 in the associated discussion of the present application (*see*, pp. 64-89). This experimental procedure is also discussed in the Declarations of Dr. Kaltenboeck annexed hereto in the evidence appendix. As described on pages 70-72 of the application, clones that contained *Chlamydia psittaci* DNA inserts that coded for open reading frames of more than 50 amino acids were identified in three rounds of screening and were considered to be potential vaccine candidates by the inventors (*see*, e.g., p. 70; Fig. 3). Fourteen particular gene fragments were identified and those gene fragment were tested in the experiment of Fig. 5 of the present application on mice. The experiment included four controls, including a positive control for genetic immunization wherein the pool of all the fourteen identified gene fragments having more than 50 amino acids was administered, a negative control wherein a pool of inserts less than 50 amino acids long was administered, a control vaccination with low dose *Chlamydia psittaci* infection that elicited a strong specific immunity against *Chlamydia psittaci* and a challenge control of mice that were completely unexposed to *Chlamydia psittaci*. The results of the experiment are detailed at pp. 70-72 and in Fig. 5 of the present application. the results clearly indicate that genetic immunization with CP4#s 1 to 5 achieved protection from *Chlamydia psittaci* better than what is achievable from natural low dose vaccination. The positive genetic immunization control pool (greater than 50 amino acids) also protected better than what is naturally achievable. Accordingly, from the experiment of Fig. 5, particular gene fragments that were effective to induce an immune response against *Chlamydia psittaci* were identified. In fact, the most highly protective gene identified in Fig. 5 was Gene No. 1 of Fig. 5 which corresponds to CP4#1 in Table 2 in Fig. 6 of the present application. The sequences of all 14 plasmids inserts were analyzed, the full *C. psittaci* genes isolated, the position of the fragments within the full genes determined, and the full genes characterized for gene terminology and function by homology search. These results are shown in Fig. 6, and are described in Example 6 with a summary in Table 2 (p. 74) and a complete listing of all sequences with SEQ ID Nos. are provided in Table 3 (p. 75-80) of the present application.

Thus, CP4#1 was sequenced and is represented by Sequence ID Nos. 6-9, wherein Sequence ID No. 6 is the original DNA gene fragment, Sequence ID No. 7 is the polypeptide fragment corresponding to the gene fragment of No. 6, Sequence ID No. 8 is the full length DNA gene that includes the gene fragment of Sequence ID No. 6; and Sequence ID No. 9 is the full length polypeptide sequence of Sequence ID No. 8. Accordingly, because Fig. 5 demonstrates a specific method of immunizing an animal including the step of administering a

Chlamydia psittaci antigen to an animal in an amount effective to induce an immune response against *Chlamydia psittaci,* and wherein the antigen comprises the sequences set forth in Sequence ID No. 7, applicants believe the method of the present invention is enabling.

The state of the prior art of making and using antigenic peptides is well known using PCR techniques for amplifying a coding sequence of the DNA of a fragment, cloning these into expression vectors, expressing the protein in any recombinant protein expression system and then purifying as a recombinant protein. Appellants respectfully assert that any person of ordinary skill in the art can prepare an antigen comprising a particular amino acid sequence, once an advantageous sequence is identified, through a particular polypeptide to polynucleotide sequence. Additionally, claim 92 recites that the antigen comprises SEQ ID No. 7. SEQ ID No. 7 is the amino acid sequence of the most highly protective gene fragment identified in Examples 1-4 in Fig. 5, namely, Fig. 5, Round 4, Gene Fragment No. 1, i.e., CP4#1. The claim is clearly enabled because Examples 1-4 in Fig. 5 demonstrate the efficacy of that particular gene fragment in conferring protection and because it is a "routine matter to convert back and forth between an amino acid sequence and the sequences of nucleic acid molecules that can encode it." In re Wallach, 378 F.3d 13320, 1334, 71 USPQ2d 1939 (Fed. Cir. 2004). Moreover, the incorporation of identified genes into commercial vaccines is enabled at Example 11, page 86, of the present invention.

Additionally, the level of ordinary skill in the art is high. The technology of genetic (DNA) immunization has been well known since at least 1992, *see*, e.g., Tang et al "Genetic Immunization is a Simple Method for Eliciting an Immune Response," Nature 356, 151-4 (1992) (Exhibit E to evidence appendix). Sub-unit vaccines that consist of one or a few proteins of a pathogen are also well known, *see*, e.g., Babiuk "Broadening the Approaches to Developing More Effective Vaccines," Vaccine 17, 1587-95 (1995) (Exhibit F to evidence appendix); and Ellis, "New Technologies for Making Vaccines," Vaccine 17, 1596-604 (1999) (Exhibit G to evidence appendix).[2] Where the high level skill in the art comes into play is the identification of the particular protein or protein fragments that actually are efficacious in conferring protection and thus can be used for a method of immunizing.

Likewise, the level of predictability insofar as identifying whether a particular sequence or gene is efficacious in immunizing is high, as the methods and protocols for

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[2] The Tang, Babink and Ellis references are all provided in the listing of references at pp. 90-98 of the present application.

determining whether or not a gene or fragment thereof provides an immune response is well known. However, there is a high degree of unpredictability in determining the particular sequences from an entire genome that will confer an immune response. Appellants note that while the amount of experimentation to practice the full scope of the claimed invention might have been extensive, it would have been routine. The techniques necessary to do so were well known to those skilled in the art. *See*, e.g., Johns Hopkins Univ. v. Cellpro, Inc., 152 F.3d 1342, 1360, 47 USPQ2d 1705, 1719 (Fed. Cir. 1988) ("test [for undue experimentation] is not merely quantitative ... if it is merely routine"). A "patent need not teach, and preferably omits, what is well known in the art." Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

Appellants respectfully assert that the present application in conjunction with the multitude of cited references at pp. 90-98 of the present application provide an abundant amount of direction to provide a method of immunizing once the particular sequences were identified. Moreover, the multitude of working examples on both mice and cows demonstrate that the amino acid polypeptide sequences of SEQ ID Nos. 7, 9, 11, 13, 27 and 29 all confer immunity. Identification of the protective genes is described on pages 64-80 in Examples 1-6, and is illustrated in Figs. 1-6. The claims for fragments and full length polynucleotide and polypeptide sequences of protected genes are based on the identification of protective fragments identified in the examples, particularly Example 5. Specific evidence for the mouse protective effect is presented in Figs. 5 and 6 for SEQ ID No. 6 (SEQ ID No. 6 is CP4#1), which is the DNA fragment corresponding to the claimed polypeptide SEQ No. 7. Table 2 of the original protective clones on page 74 of the application identifies all the corresponding Chlamydial genes. All sequence identification numbers of clones containing protective gene fragments or the corresponding polypeptides, full length protective genes in the corresponding polypeptides are shown on Table 3 on pages 75-79 of the present application.

Appellants respectfully assert that one of ordinary skill in the art can simply make and use the identified antigens and antigenic fragments taught by the specification, particularly those of SEQ ID Nos. 7, 9, 11, 13, 23 and 27 and thereby induce a protective immune response by following the teachings of the art and the specification. Even an extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance, In re Colianni, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). Applicants

strongly assert that the present specification provides ample amount of direction to one of ordinary skill in the art.

In sum, applicants respectfully assert that the present specification provides ample enablement for a method of immunizing an animal in an amount effective to induce an immune response of applicants' *Chlamydia psittaci*. The instant specification provides ample enablement to produce such immune response with *Chlamydia psittaci* antigens comprising the polypeptide sequences as set forth as SEQ ID No. 7, 9, 11 and 13. Favorable consideration is respectfully requested.

E. Conclusion

Favorable consideration of this Appeal and removal of the rejection under 35 U.S.C. § 112, ¶1, for lack of enablement is earnestly solicited.

Respectfully submitted,

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CLAIMS APPENDIX

In accordance with 37 C.F.R. §41.37(c)(1)(viii), this Claims Appendix sets forth the claims involved in the Appeal, namely claims 92, 94, 95 and 104-121.

Claims 1-91 (canceled)

Claim 92 (previously presented): A method of immunizing an animal comprising the step of:

administering a Chlamydia psittaci antigen to an animal in an amount effective to induce an immune response against Chlamydia psittaci; wherein the Chlamydia psittaci antigen comprises the amino acid sequence as set forth as SEQ ID NO:7.

Claim 93 (cancelled)

Claim 94 (previously presented): The method of claim 92, wherein the method further comprises the step of:

administering a second Chlamydia psittaci antigen to an animal in an amount effective to induce an immune response against Chlamydia psittaci; wherein the second Chlamydia psittaci antigen comprises the amino acid sequence as set forth as SEQ ID NO: 9, 13, 23, or 27.

Claim 95 (previously presented): The method of claim 92, wherein the method further comprises the step of:

administering a second Chlamydia psittaci antigen to an animal in an amount effective to induce an immune response against Chlamydia psittaci; wherein the second

Chlamydia psittaci antigen comprises the amino acid sequence as set forth as SEQ ID NO: 11, 17, 23 or 27.

Claims 96-103 (canceled)

Claim 104 (previously presented): The method of claim 92 wherein the step of preparing a Chlamydia psittaci antigen further comprises preparing the Chlamydia psittaci antigen in a pharmaceutically acceptable carrier.

Claim 105 (previously presented): The method of claim 94 wherein the steps of preparing a Chlamydia psittaci antigen and preparing a second Chlamydia psittaci antigen further comprises preparing the Chlamydia psittaci antigen and the second Chlamydia psittaci antigen in a pharmaceutically acceptable carrier.

Claim 106 (previously presented): The method of claim 95 wherein the steps of preparing a Chlamydia psittaci antigen and preparing a second Chlamydia psittaci antigen further comprises preparing the Chlamydia psittaci antigen and the second Chlamydia psittaci antigen in a pharmaceutically acceptable carrier.

Claim 107 (previously presented): The method of claim 92 wherein the animal is a bovine.

Claim 108 (previously presented): The method of claim 94 wherein the animal is a bovine.

Claim 109 (previously presented): The method of claim 95 wherein the animal is a bovine.

Claim 110 (previously presented): The method of claim 92 wherein the animal is a human.

Claim 111 (previously presented): The method of claim 94 wherein the animal is a human.

Claim 112 (previously presented): The method of claim 95 wherein the animal is a human.

Claim 113 (previously presented): The method of claim 92 wherein the animal is a mammal.

Claim 114 (previously presented): The method of claim 94 wherein the animal is a mammal.

Claim 115 (previously presented): The method of claim 95 wherein the animal is a mammal.

Claim 116 (previously presented): The method of claim 94 wherein the step of administering the second Chlamydia psittaci antigen comprises administering the second antigen simultaneously with the administration of the first antigen.

Claim 117 (previously presented): The method of claim 94 wherein the step of administering the second Chlamydia psittaci antigen comprises administering the second antigen subsequent to the administration of the first antigen.

Claim 118 (previously presented): The method of claim 94 wherein the step of administering the second Chlamydia psittaci antigen comprises administering the second antigen prior to administration of the first antigen.

Claim 119 (previously presented): The method of claim 95 wherein the step of administering the second Chlamydia psittaci antigen comprises administering the second antigen simultaneously with the administration of the first antigen.

Claim 120 (previously presented): The method of claim 95 wherein the step of administering the second Chlamydia psittaci antigen comprises administering the second antigen subsequent to the administration of the first antigen.

Claim 121 (previously presented): The method of claim 95 wherein the step of administering the second Chlamydia psittaci antigen comprises administering the second antigen prior to administration of the first antigen.

EVIDENCE APPENDIX UNDER 37 C.F.R. § 41.37(IX)

A. Declaration Under 37 C.F.R. § 1.132 of Akira Takashima, M.D., Ph.D.; submitted March 10, 2005; entered in Office Action mailed May 31, 2005.

B. Declaration Under 37 C.F.R. § 1.12 of Dr. Bernhard Kaltenboeck; submitted April 17, 2007; entered in Office Action mailed June 29, 2007.

C. Declaration Under 37 C.F.R. § 1.132 of Dr. Bernhard Kaltenboeck; submitted August 8, 2007; entered in Office Action mailed September 19, 2007.

D. Chart provided during October 23, 2007 interview and submitted in October 26, 2007 Reply to Advisory Action correlating *C. psittaci* gene fragment numbers of Fig. 5 to CP4# designations in Fig. 6 and Table 2; entered in Office Action mailed January 21, 2008.

E. Tang et al "Genetic Immunization is a Simple Method for Eliciting an Immune Response," Nature 356, 151-4 (1992); considered by the Examiners on October 2, 2004 (*see*, PTO From 1449 with Office Action mailed November 10, 2004).

F. Babink, "Broadening the Approaches to Developing More Effective Vaccines," Vaccine 17, 1587-95 (1995); considered by the Examiners on October 28, 2004 (*see*, PTO Form 1449 with Office Action mailed November 10, 2004).

G. Ellis, "New Technologies for Making Vaccines," Vaccine 17, 159601604 (1999); considered by the Examiners on October 28, 2004 (*see*, PTO Form 1449 with Office Action mailed November 10, 2004).